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ABSTRACT

The author reviews the literature and makes tentative conclusions concerning the physiological correlates of learning and memory. Particular attention is given to the issues of spinal cord learning, subcortical learning, cerebral cortex learning, localization of learning within the brain (specificity vs. non-specificity), and association areas (specific areas where learning is possibly controlled). Physiological changes within the brain resulting from learning are also explored. (BWP)

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THE PHYSIOLOGICAL CORRELATES OF LEARNING

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Autumn Semester,1973
Physiological Processes
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INTRODUCTION

Since human beings have inhabited the earth the seemingly innate curiosity of this species has perpetuated its search for understanding. The infinite array of questions brought forth by numerous individuals has led to explorations of almost the total environment, from the most minute details to the vastness of space. With each discovery knowledge grows and for better or worse life is altered.

Perhaps of most importance to the survival of the species is the curiosity which has led humankind to "desire" to know itself. The human body has been broken down, studied piece by piece, reassembled and studied as a whole. Needless to say medical advances have made life, to different degrees, easier to live.

At the base of this ability to perform such creative feats lies an unsolved mystery. One that has plagued and stimulated scientists for centuries. Decoding the organ, which places homeo sapiens apart from other animals, the human brain, has not yet been accomplished. Nonetheless, advancements are being made and questions are being slowly answered.

To the early Greeks the mind was perceived as a separate entity, "the seat of knowledge." To them it comprised a tablet inscribed by experience (Stevens, 1971).

Speculations, followed by intense study and experimentation has only begun to describe or explain this "seat of knowledge." Thoughts, memory and learning are ever present and constantly functioning, but how they perform remains unexplainable.

Hampered by lack of technology and the need for communication between laboratories the progress is painfully slow. Contemporary scientists have indeed generated much controversy with their recent claims. It is, however, like a massive jigsaw puzzle with some essential pieces missing. Gradually the fragments are being found and in time conceivably there will be a complete answer to the pertinent questions concerning the ability to "know."

In the past few decades this line of inquiry has been working in a flexible framework. The major aspects of this study appear to center around specific topics. Localizing the physical structure of the brain and the functions of it's parts, as they pertain to learning was one of the earliest areas of interest to the scientist. Another fundamental area of study is that of the active and structural theories of the memory trace. Within the study of the memory trace two particular factors have been focused on; the role of biochemicals between neurons and the possibility of a 'macromolecular theory' of learning.

It is the intent of this paper to review these afore mentioned areas in some detail. The rapidity with which research is done makes todays facts or findings impetus for tomorrows new discoveries. For this reason some of the reports I will refer to could be obsolete by the time they are read. Nevertheless the attempt will be made.

DEFINITIONS AND ASSUMPTIONS

Learning has been defined in many ways by people involved in psychology, philosophy, education and other sciences. Common to these definitions is the idea of a relatively permanent increase

in response strength to a somewhat specific stimulus (Miller, 1967; Hilgard and Bower, 1966) This would appear to be the end result of learning. The steps that occur within this process, memory, problem-solving, attention and so on must also be considered in the whole definition.

The general assumption of scientists involved in searching for the physical processes of learning is that learning does correlate with some change in the nervous system. According to Krech et. al.(1958) the pattern of cortical activity in response to a stimulus, is different after a person has acquired a new expectation or habit from what it was prior to acquisition. Or as Stevens (1971) describes it more simply; intellectual exercise leaves a residual change in the brain.

From this premise, learning defined and the general assumptions, I will begin my review with the structural characteristics of the brain that have been found to be involved in learning.

STRUCTURE AND FUNCTIONS OF THE BRAIN AS RELATED TO LEARNING

As early as 1824 Pierre Flourens, a french physiologist, did the first experiments relating behavior to the brain. His conclusions are still quite characteristic of contemporary thought and brain research. They are as follows:

1. The brain is made up of several organs, each with its own functions.
   The cerebellum is the "seat of the principle which coordinates locomotor motion."
   The cerebrum is the "seat of intellegence."
2. The cerebrum is functionally indivisible.

3. Various intellectual faculties are all one because they share a common structure in the brain.

As will be seen in the following pages some of Flourens' conclusions will be both modified and expanded due to research findings since his initial experiments. In general, his conclusions are relevant to and in agreement with many attempts to locate where learning occurs and are, therefore, worth mentioning at this point.

Attention has primarily been focused on the cerebral cortex, the highest level of the nervous system, in attempting to find the specific areas involved in learning. However, research and subsequent findings related to the spinal cord and the subcortical level cannot be overlooked. (See figure 1, for location of different levels). The question asked concerning this research was typically: Can learning take place without the involvement of the brain? Results of this work tend to answer in the affirmative. A closer examination of these studies follows.

Spinal Cord Learning

Studies at the spinal level have reported both positive and negative results regarding the acquisition of response with only the spinal cord functioning. The usual subjects for studying this possibility are "spinal animal." These are experimental animals whose spinal cords have been completely cut from the brain. Comparatively, human paraplegics, who have undergone surgery disconnecting the lower half of the body from the brain, have also been observed with regard to this phenomenon. Conditioned response learning has been found to occur in both of these instances,

providing the stimulus and response involve only the lower body (Culler and Shurrager, 1940; W.N. Kellogg, 1947).

Such findings reveal that the integration of incoming sensory stimulus and outgoing motor impulses are controlled by the spinal cord alone. Although negative findings give cause for reservation when considering this type of learning. Regardless, it must also be remembered that this is only the simplest form of learning and the mechanisms involved in complex behavior is to be sought in other areas of the nervous system.

Subcortical Learning

Another area where the process of learning has been explored is the subcortical area, a section of the brain directly above the spinal cord. Studies done with "decorticated" animals tend to be in agreement. Removal of the whole cortex does not destroy the ability of the animal to learn primitive problem solving tasks (Bromily, 1948). Conditioned learning has also been shown to occur when only the subcortical level is functioning (R.W. Doty, 1961; for an extensive review of this topic see R.S. McCleary and R.Y. Moore, 1965).

Here again this mechanism alone cannot accomplish the acquisition of complex patterns of behavior. In the next section the highest level of the nervous system will be investigated, the cerebral cortex.

Cerebral Cortex Learning

Due to the complex structure of the cerebral cortex it has been most readily referred to as the "locus of learning" (Krech et. al., 1958). Its billions of neuronal cells and infinite

number of patterns and sequences of nerve impulses equips it with everything needed for the integration of activity. In figure #2 it is seen that as intellectual and adaptive behavior become more essential to the organism this area increases in complexity and in some cases size. In humans this 'grey matter' is most complex, which further supports the view that intellegent learning occurs in the cortex.

In addition to this seemingly strong support regarding the cerebral cortex it must also be mentioned that there is an equally strong possibility that the centers below the cortex are essential components in the learning process. Consequently, scientists have not sought "the" locus of learning. Instead they have tried to understand each of the many areas of the cortex in isolation from the others.

Localization: "specificity" vs "non-specificity"

Localizing the specific areas of the brain, which are involved in different patterns of behavior was stimulated by the technological discovery of the electroencephalograph (EEG). Moreover, Hans Berger in 1924 demonstrated that attaching an EEG to the skull produced minute amounts of electrical responses, which varied according to the behavior of the subject (D.E. Wooldridge, 1963). Observation of brain damaged humans has also proven to be informative with regard to localization. Patients display varying forms of behavior, depending on where the damage is centered. Experiments done by removing specific areas have resulted in findings consistant with these above mentioned occurances (D.O. Hebb and W. Penfield, 1940; L.J. Kornash and W.J. Gardner, 1940).

The major theories of localization are divided into those who either support non-specificity or specificity of cortical functions. A review of some of the findings in each of these areas follows.

K. S. Lashley (1950) has been associated with the non-specificity theory. Cortical ablations of 1,000s of rats, trained and tested in miles of mazes led him to state the following:

> This series of experiments has yielded a good deal of information about what and where the memory trace is not....It is difficult to conceive of a mechanism which can satisfy the conditions set for it (learning). Nevertheless, in spite of such evidence against it, learning does sometimes exist (Lashley, 1950).

A negative statement to say the least! On the positive side of Lashley's findings he proposed the probability that there was "equipotential" in the regions of the brain. He found that a lesion of a certain size in one part of the brain has the same effect as a same size lesion in another area. He also introduced the term "mass-action," which referred to the finding that not which areas were removed, but how much was removed was what caused the effect. Memories and learning areas are, therefore, diffused throughout the cortex.

Proponents of the specificity view limited these conclusions by raising additional questions. In summary their experiments led them to deduce that learning involves the integration of the specific sensory and motor areas. The degree of complexity of the task predetermines the need for certain areas to be present during acquisition. The larger the lesion the more, partial or whole, areas are destroyed and thus the less ability the brain has to integrate the sensory input (I. Krechevsky, 1936).

The second and possibly most important concept of this theory is that of compensation. This refers to the redundancy and plasticity of the brain, which enables destruction to occur without crucial impairment of learning or behavior. When one sensory modality is destroyed often the other parts will adapt and take over (W. Penfield and L. Roberts, 1959).

Evidence most supportive of specific areas of learning has been derived from studies centering around the "association areas" of the cerebral cortex. Advocates of the specificity theory have accumulated an extensive amount of information pertaining to these areas. The next section will discuss these findings.

Association Areas

As specific areas have been found to control motor and sensory functions (Lashley, 1950) the association areas have been designated as possible areas, where learning is controlled. This area, which increases in size as the organism moves up the phylogenic scale, is divided into two parts; the posterior association area (PAA) and the frontal association area (FAA) or the frontal lobe. (see figure 3).

As can be seen in the diagram the PAA is surrounded by sensory areas. Lesions here lead to defecits in learned behavior involving sensory discrimination. Also separate regions within the the PAA have been shown to be important to the various sensory inputs. That is, input from the sensory modalities in some tasks must enter and combine with various areas of the PAA before a proper response can be made.

The split-brain technique used by R. W. Sperry (1961) has furthered the study of this cortical area. By adding the split-

brain procedure to lesions made in the cortex, information regarding learning was established. In visual discrimination tasks more areas of the cortex are involved than in mere perception. A descriptive diagram appears in figure 4, which concisely summarizes this type of experiment.

These findings which were done with experimental monkeys have also been confirmed with humans who have suffered brain damage. There is reason to believe that the PAA in humans also contains the primary sensory areas. Injury to the different subareas of the PAA is followed by various forms of agnosia, an inability to recognize familiar objects. The function the sensory input plays in integrating the various senses seems to be impaired. However, simple sensory functions are not lost (Teuber, 1959).

The FAA has also been the subject of intense study. Using animals as subjects (S) lesions of the FAA have caused an effect in the ability to use sensory information in some adaptive behavior.

The common method employed when dealing with this area is the "delayed-response problem." As defined by Krech et. al. (1969) this involves a task in which the S has to respond in terms of a stimulus that is no longer present. If the Ss frontal lobe is destroyed the S fails to accomplish this task.

Interpretations of this phenomenon have taken three different approaches which are relevant to these findings. This deficit in learning has been attributed to the function of the FAA as it is related to memory, attention and persevaration. There is good evidence to support all three of these views. (See Krech et. al., 1969 for further explanation).

In general the explanations for the apparent disagreement

among scientists are: (1) the processes of memory, attention and perseveration may not be sufficiently understood and may in fact really be the same process and (2) the PAA itself may also not be adequately understood. These are indeed vague explanations for quite blatant discrepencies, but it does serve to exemplify an important fact. There is a vast amount of knowledge yet unknown to those who are attempting to localize cortical areas. Further and more intense investigation will only serve to rectify this and will undoubtedly take many more years of work.

Comparatively, more is known about the frontal-lobe of the human brain and its role in learning, due to the use of frontal lobotomys used in treating psychotic patients. Removal of the frontal lobes or transections of their connections effects the patients ability to learn complex tasks, but not complete loss of intellectual ability is experienced. There does appear to be some association between the emotional desires and intellectual activities (P.M. Tow, 1955). It has also been shown that physical processes, involuntary processes, are not controlled by this area (D.O. Hebb, 1945). In summary Pribram (1962) has referred to the PAA in human's as being in control of "intentional" behavior and voluntary responses.

Perhaps the most impressive knowledge of the PAA which has been acquired through experimentation is the localizing of the speech areas of the cortex. Karl H. Pribram (1959) through electrical stimulation of various parts of the entire cortex (PAA and PAA) has located areas in the brain which appear to be involved in the process of speech. (see figure 5). He has further found that these areas only exist in the left hemisphere of the normal brain.

(Some left-handed people have been found to have speech areas in the right-hemisphere).

Speech is an acquired function and therefore, learned by each speaking individual. Yet the speech areas appear to almost always occupy the same sections of the brain in each individual. This would lead to the assumption that the learning process must somehow make it's physical impression in a predetermined area. These findings serve a dual purpose. First they support the specificity of certain parts of the brain and secondly the idea that there is a physiological correlate to learning is also strengthened.

Aphasia is a speech disorder suffered by people with damage to these areas. They exhibit different disorders depending on where and when the damage occurs. By observing people with aphasia it was found that a problem occurs in the production of speech when the damage is in the frontal lobe. When the patient is unable to understand or recognize spoken language the damage is usually in the PAA. These two types of aphasia are labeled motor and sensory aphasia respectively.

Findings such as this present even more evidence in a more detailed form for the possibility of specific areas which perform specific functions within the brain. It should not be surprising that the literature suggests that learning areas do exist since other involuntary reactions have been localized. The distinction between these areas that control involuntary actions and those that control learning is that somehow these learning areas must be developed independently.

This comparatively short review of the importance of the dif-

ferent neural structures has not answered the question of where learning actually occurs in the nervous system. However, it does reinstate the fact that when dealing with the brain one is dealing with a most complex organ. Yet, it also strengthens the idea of a physical basis for learning. As Krech et. al. (1969) have stated knowing where learning takes place may be accomplished when we find what takes place during learning. This then is the next major topic to be reviewed.

PHYSIOLOGICAL CHANGES WITHIN THE BRAIN

Ascertaining what takes place in the learning process may be even more complicated to conceptualize, investigate and report than where it happens. Factoring out the numerable variables effecting the complex process of learning is a major obstacle in the study of it's physical basis. Through this somewhat trial and error procedure progress is being made.

Memory Trace: active or structural

In the earlier part of the century the idea of the memory trace was introduced. This was an important development since it led to further hypothesizing and research regarding the constituents of learning.

Primarily the memory trace is the storage of past experience and also a majpr component in learning. Theoretical explanations of the memory trace are divided into two lines of thought. First, the structural trace, a permanent change occurs in the physical or chemical properties of the individual neurons. Secondly, the active

trace, a pattern of neural activity is set up within the brain, as a result of a "learning" experience.

The progress which has been made in the recent years concerning these two positions has essentially been accomplished by utilizing three approaches, These approaches are as follows:

1. The application of agents, chemical or physical, that interrupt or abolish memory.
2. Studies of chemical changes in the central nervous system during learning.
3. Experiments of chemical transfer of learned information.

Each of the previously mentioned positions regarding the memory trace and these three approaches will be reviewed in the succeeding pages.

The active trace theory was held by K.S. Lashley (1950). His theory, referred to as the "reverberating circuit," purposes that a closed loop of neurons is formed within the cortex. A series of neural impulses continuously firing. This circuit remains in the nervous system after the external stimulus, which initially caused the impulse to enter the nervous system has gone. The final result being a permanent, new aspect of the brain's pattern of electrical activity, i.e. a memory trace. (see figure 6).

D.O. Hebb (1949) further explained this theory. As he has stated it, there is a recurrent active trace, which is responsible for gradually developing a permanent structural change, different from the original. This memory process has commonly been referred to as consolidation.

The active trace in both Lashley's and Hebb's theory is what has been called, short-term memory. This phase of memory is short

lived and easily disrupted, as will be seen directly. The later stage of Hebb's theory, the permanent structural change, has been labeled long term memory. It is the major component of learning and has been investigated by a number of scientists with a substantial amount of success.

The three afore mentioned approaches have been the primary instruments used in studying the two stages of memory. Both the active and the structural trace has undergone further conceptualization and modification. To report all the advances would take volumes. For this reason I will attempt to report only the major findings of each of these methods.

Application of Agents that Interrupt or Abolish Memory

The structural theory, involving the recurrant electrical activity of neurons, was not completely accepted. It was thought that if memory did consist of electrical activity then it should be disrupted by electrical activity imposed upon the brain after learning.

Duncan (1949) performed an experiment giving an electroshock to rats during the course of learning. The task was a simple avoidance and the rat was given only one trial per day. Highly significant effects occured when the convulsion was imposed within a few minutes after a learning trial. A shock given an hour or more after a learning trial had no effect. Complete memory of the task was retained. Long term memory was not electrical.

Evidence from latter studies using inhibitors of protein synthesis have supported the theory that information in the long term memory might be stored by a chemical. If RNA synthesis was

blocked by actinomycin-D, a metabolic inhibitor, memory consolidation was interfered with (Arganoff et al., 1967). Although, these animals were able to learn the required problem, they could not retain it when actinomycin-D was injected shortly after acquisition.

Similar results have been found by Flexner et al., (1963). After training mice in a Y-maze they injected the animals with puromycin. Puromycin is an antibiotic that blocks the protein synthesis in ribosomes. Throughout a series of like experiments mice were injected between 1 and 60 minutes after training and retested between 3 and 4 days after treatment.

The findings were that this substance was not effective after a delay, but had to be given within the same period of time during which the ECS was effective.

Conclusions drawn from these inhibitor studies purport that long term memory requires a synthesis of protein, preceeded by RNA synthesis, which must take place during the consolidation period. These conclusions have been interpreted in two ways. First, this new synthesized material is needed only for growth, the change then regarded as quantitative. The second explanation is that the new molecules have coded into them information essential for the storage of learned information. This would be a qualitative change of different molecules with their composition corresponding to the acquired information. The transfer concept is based on this second explanation and will be discussed shortly.

The inhibitor studies have been beneficial to the progress being made in the study of learning primarily by further confirming the two stage theory of memory. The second approach will

be seen to expand upon this by focusing on the chemistry involved in this process.

Chemical Changes in the Central Nervous System

The procedure involved in how molecules go about registering and storing information, which occurs during learning is the next topic to be discussed. This qualitative change in molecules has been analyzed by employing the second approach, studying the change in brain chemistry aesociated with learning experiences.

A series of experiments done by Rosenzweig et al. (1960) is an example of this. They intended originally to deal with the relationship between intelligent animal behavior and brain chemistry. While investigating this it was also found that the anatomy of the itself was also effected. This finding will be looked at first.

The general design used was to place pairs of rat pups, which were littermates, into two different environments. Group I rats were placed in an "impoverished environment," (IE). This consisted of solitary confinement, a small dimly lighted cage with none of the stimulation that would be found in social living. Group II rats were put in an "enriched environment" (EE). The EE was a large cage with many other rats present, well lighted and plenty of "rat toys." These rats were also given training in a series of maze tasks, which further stimulated their development.

After 80 days each of the littermates were killed and their brains were analyzed and compared for cerebral differences. Their findings were quite extensive and revealing concerning their preliminary question. Also some unexpected results were found. A summary of their results appears in figure 7 on the following page.

Figure 7

Results of the comparative analysis of Group I (IE) and Group II (EE) rats.*

Differences in the EE Brains as Compared to the IE Brains

size and weight	a. bigger cortex b. 4% heavier c. specific areas of brain also heavier
enzymatic differences (finer analysis)	a. an over-all increase of ChE[1] and AChE[2] b. ChE increased only in relation to greater weight of cortex c. AChE decreased per unit weight
glial and neuron cell analysis	a. increase in glial cells[3] b. fewer neurons per unit weight.[4]
neuron changes	a. neurons were enlarged b. nuclei increased in size
capillary changes	a. increased in diameter[5]

*The major effects on the EE brains are given except in the 'enzymatic difference' category, which was an over-all effect.

1. Cholinesterase
2. Acetylcholinesterase (1 and 2 are enzymes which breakdown neuron transmitter acetylcholine.)
3. ChE is associated with glial cells therefore a greater amount of ChE.
4. AChE is associated with neurons therefore a decrease of AChE.
5. A physical response to a need for more blood activity in the brain.

Further experimentation has demonstrated that the IE rats are able to develop EE equivalent brains when placed in the "enriched environment" for a period of time (Krech et. al., 1964).

These are most impressive findings concerning the physiological changes correlated with learning. Unfortunately it does not answer the over-all question of what causes such changes to take place. Expanding on the biochemical aspects of their previously mentioned study Krech and his colleagues have searched further for these answers. (Rosenzweig et al., 1962, 1968)

a. Chemical Changes at the Synaptic Junction

An earlier assumption held by D. O. Hebb (1946) was that the ease with which activity in an axon can excite the adjoining neuron depends on how easily the appropriate synapse can be crossed. According to Hebb the terminal bouton at the synaptic end of the stimulating neuron "grew" closer to the receiving neuron as a result of the nerve impulses. This assumption is purely theoretical but has been somewhat scientifically supported by the study which follows.

According to the hypothesis of Krech et. al. (1960) if (1) neuronal activity depends on synaptic transmission and (2) the synaptic transmission requires chemicals then (3) the efficiency of the neuronal activity, in learning, should be related to the activity level of the transmitter substance in the brain. Unfortunately, their results are not conclusive. However they are worth reviewing, due to some of their significant findings.

The chemicals measured in the brain's of rats, which had either been trained or untrained, were Acetylcholine (ACh) and Acetytcholinesteras

(AChE). ACh is the transmitter substance and AChE is an enzyme that breaksdown ACh.

In measuring the adaptive behavior of rats in a learning situation they first looked for a relationship between; adaptive behavior measures and the degree of AChE activity in the brain. They assumed the AChE activity would indicate the amount of synaptic transmission. A high level of AChE would reveal a high degree ACh activity, which was presumed to be learning. A positive correlation between adaptive behavior and AChE was found in their first experiment, but replications sometimes found a negative correlation.

An explanation of these negative results, a large amount of AChE correlated with poor adaptive behavior, is that the AChE brokedown the ACh too quickly. The ACh, therefore, wasn't able to have it's effect on transmission.

In a second series of experiments these same experimenters (1960) considered the ACh level relatively to the amount of AChE. Their finding was that rats with higher "ratios" of ACh to AChE had superior learning behavior. This study seems to substantiate the idea that the synaptic substance does in fact have an effect on learning.

Additional studies have been done attempting to change the level of ACh or AChE. Deutsch et. al. (1966) prevented AChE from destroying ACh by administering an antichlorinesterase. This drug allowed an increase in ACh to occur. Their experiment showed that there is a certain amount of ACh which could be considered optimal for memory of simple maze tasks taught to rats. If this drug is given when a problem was not learned well it made the

problem easier by supplying more ACh. However, when a task had been well learned and the drug was given, which allowed for a large amount of ACh to be available, the injection caused a memory loss. Therefore, it appears that there is also a level of ACh which can be detrimental to learning. It has been suggested that perhaps the neurons are put into a condition where they are continually stimulated and the synapse is unable to effectively transmit the incoming information.

Having looked at the chemical changes at the synaptic junction I will now move on to the possibility of a change in chemicals within the neuron.

b. Chemical Changes in RNA

Evidence that there is a qualitative difference in the molecules which form during learning also come from analyzing the effects of learning on the RNA synthesis in the central nervous system. A review of the literature seems to suggest that a change in RNA does occur after learning. A review of this major work follows.

In an experiment done by Hyden et. al (1962) the single neurons of RNA were analyzed. They found that different learning experiences resulted in an increase in the amount of RNA plus a change in the composition of the RNA. Control animals who were exposed to sensory stimulation without learning had an increase of RNA with no compositional change.

Similar findings are reported by a number of different experimenters using a variety of subjects and methods (Sashoua, 1968; Zemp et. al., 1966, 1967) The primary obstacle in the complete validation of this work is the lack of sophisticated procedures

which would permit replications of this work in other laboratories. Also, the problem of differentiating what is causing the RNA base ratio change, learning, stress, activity etc., has not been completely verified. These are only a few of the complications involved in the chemical analysis of RNA.

According to McConnell and Golub (1971) in a review of the empirical issues involved in this type of analysis, there are three variations of this general approach used for isolating the chemical correlates of memory. They are "memory transfer," pulse labeling and successive competition hybridization. A short explanation of these follows.

McConnell et. al. (1961) while working with trained flatworms observed an unexpected event. When trained flatworms were sectioned and allowed to regenerate the newly formed worms showed a retention of the original task trained to the previously whole worm. Of vital interest was that only one of the newly developed flatworms was formed from the section containing the original brain. Subsequent experiments showed that worms fed the trained worms and later trained themselves, acquired a conditioned response significantly faster than those worms ingesting untrained worms.

Corning and John (1961) expanding upon this initial finding indicated that the substance responsible for the transmission of acquired information is probably RNA. Furthermore the effect can be eliminated if RNA extracted from the trained donor worms is incubated with RNAse before injecting into the recipient worms.

The second approach was begun by Zemp and his colleagues (1966, 1967). By using radioactive labeling procedures, they demonstrated increased incorporation of labeled forerunners of

RNA during a learning experience in mice. Their findings of a change in the synthesis of RNA during learning could not be conclusively stated because they did not include a control group. Due to this their observed differences could have been attributed to a number of other factors. However, their research stimulated Adair and his experimental team (1968) to replicate this study and to include a control group. The results of this experiment were similar to those of Zemp et. al. and the increased synthesis of RNA as an effect of learning was further supported.(1966)

The third approach used by Gaito et al. (1968, 1969). In this approach DNA-RNA successive competition hybridization procedures are applied to learning situations to determine whether a new species of RNA is synthesized during learning.

This procedure has come from work with bacteria and may not be transferable to memory studies. If, however, the work of Gaito can be repeated this type of assay may prove to be valuable.

Not found in all of the approaches used by those investigating the chemical effects of long term memory these three approaches do at least offer a direct method. Investigators using these approaches have a clear cut way to refer biochemical changes occurring during learning to memory mechanisms.

This brings us to the final chapter in the continuous search for the mechanisms of learning. The chemical transfer of the information derived during learning.

Chemical Transfer of Learned Information

As stated by Krech et. al. (1969) the claims of these studies are in general, that specific memories can be transfered from

one animal into another by taking RNA from the brain of a trained animal and injecting it into an untrained animal; the untrained then shows a "memory" for what the first animal had learned. Needless to say if these results, are substantiated they could prove that the exact nature of memory is coded as a specific RNA.

In attempting to deal with this vast amount of research I have dicided to present the three major questions the experimenters must deal with and in general their conclusions.

As stated by McConnell and Golub (1971); "Since 1965 when researchers attempted to apply the memory transfer paradigm, initially used with the planarian, to mammals the controversy has continued." Both positive (Babich et. al. 1965; Ungar et. al., 1965) and negative (Byrne et. al., 1966) effects were found using essentially the same procedure.

Mammalian transfer studies have been repeated over 100 times in about thirty different laboratories. This work has generated much dispute centering around 3 questions: (1) Is the transfer effect a reliable, repeatable phenomenon? (2) How specific is the effect? (3) What is the active substance(s) mediating the effect?

In regards to the first of these questions, James A Dyal (1971) in reviewing an ample amount of the research since 1965 has attempted to make some inferences concerning the reliability. The major problem, he has found, in assessing the laboratory exporiments is the fact that some labs are able to replicate while others fail to do so. Dyal has suggested that 3 considerations should be kept in mind when making inferences about the reality of the phenomenon:

1. Given the condition of relative ignorance regarding the critical parameters for obtaining the phenomenon together with the likelihood that the phenomenon is dependent upon complex interactions among multiple variables, it does not seem unlikely that difficulties will be encountered in replicating procedures and results within a given laboratory as well as between laboratories.

2. Under conditions of low replicability within and between laboratories it becomes meaningful to evaluate the phenomenon by reference to the totality of relevant data.

3. As a consequence of both statistical and methodological considerations a significant positive result must be given more weight than a null result when toting up the subjective probabilities.

Taking further from the work of Dyal I have attempted to "successfully replicate" a list of studies done with the transfer phenomenon. Within this list the number of positive, negative and equivocal effects have been reported. This may appear to be a rather insufficient way to report the reliability of this approach, but regarding the vast amount of material I find it to be perhaps the most parsimonious method. This list appears in figure 8 on the next page.

Taking note of the tallied scores in the chart and given the three considerations previously mentioned Dyal has concluded that "the memory effect is a real phenomenon!"

Subsequent studies will undoubtedly lend either more support to this or detract from it. However, at this point I am inclined to agree with Dyal. Readers are invited to make their own decisions.

The second question of specificity can be stated quite simply! When a transfer effect is obtained or observed what exactly is being transfered to the recipient? As in all other phases of this research their is a large number of factors to consider. The transfer

(figure #8)

Categorization of published and unpublished experiments on memory as supporting the positive effect (+), null effect (-) or equivocal (0).

Experimental report	+	-	0	Experimental report	+	-	0
Adam and Faiszt (1967)	7	5	0	Gurowitz (1968)	0	2	0
Albert (1966)	0	1	0	Halas et al. (1966)	0	1	0
Allen et al. (1969)	0	1	0	Hayes (1966)	0	1	0
Babich et al. (1965a)	1	0	0	Herblin (1970)	3	0	0
Babich et al. (1965b)	1	0	0	Hoffman et al. (1967)	0	1	0
Beatty and Prey (1966)	0	1	0	Hutt and Elliott (1970)	0	1	0
Bonnett (1967)	1	1	0	Jacobson et al. (1965)	1	0	0
Branch and Viney (1966)	0	1	0	Jacobson et al. (1966a)	1	0	0
Braud (1970)	2	0	0	Kimble and Kimble (1966)	0	1	0
Byrne et al. (1966)	0	180		Kleban et al. (1968)	1	0	0
Byrne and Samuel(1966)	4	0	0	Krech et al. (1967)	-	-	-
Byrne and Hughes (1967)	1	-	-	Lagerspetz et al.(1968)	0	2	0
Caran and Nutter (1966)	1	0	0	Lagerspetz (1969)	1	2	0
Chapouthier and Ungerer (1969)	1	1	0	Lambert and Saurat (1967)	0	1	0
Chapouthier et al.(1969)	2	1	0	Luttges et al. (1966)	0	8	0
Corson and Enesco (1968)	0	8	0	McConnell et al. (1970)	8	1	1
Daliers and Rigaux-Motquin (1968)	8	0	0	Malin et al. (1970)	1	0	0
Daliers and Giurgéa(1971)	1	0	0	Miller (1967)	0	2	0
De Balbian Verster and Tapp (1967)	0	2	0	Miller et al. (1969)	0	5	0
Dyal and Golub (1967)	0	0	1	Moos et al. (1969)	1	0	0
Dyal et al. (1967)	2	0	0	Nissen et al. (1965)	1	1	0
Dyal and Golub (1968)	1	1	0	Reinis (1965)	1	0	0
Dyal (1969)	0	1	0	Reinis (1968)	1	0	0
Dyal and Cornell (1969)	1	0	0	Reinis and Kolousek(1968)	1	0	0
Dyal and Golub (1969)	0	0	1	Reinis(1969a)	1	0	0
Dyal et al.(1969)	1	1	0	Reinis(1969b)	1	0	0
Dyal and Golub (1970a)	0	1	0	Reinis and Mobbs(1970)	1	1	0
Dyal and Golub (1970b)	0	1	0	Revusky and De Venuto(1967)	0	0	1
Essman and Lehrer(1966)	0	0	1	Rønsaard-Petersen et al. (1968)	3	10	0
Essman and Lehrer(1967)	1	0	0	Rosenblatt et al. (1966a)	2	0	0
Faiszt and Adam (1968)	4	0	0	Rosenblatt et al. (1966b) (1966c)	4	1	2
Fjerdingstad et al. (1965)	1	0	0	Rosenblatt and Miller (1966a)	3	4	0
Fjerdingstad (1969a)	1	0	0	Rosenblatt and Miller (1966b)	3	0	0
Fjerdingstad (1969b)	3	0	3	Rosenblatt (1970)	1	-	-
Fjerdingstad (1969c)	4	0	0	Rosenthal and Sparber (1968)	1	0	0
Fjerdingstad et al.(1970)	2	0	0	Rucker and Halstead (1970)	1	2	1
Gay and Raphelson(1967)	2	0	0	Smits and Takemori (1968)	0	4	0
Gibby and Crough (1967)	1	0	0	Theologus (1967)	0	1	0
Gibby et al. (1968)	1	0	0	Tirri (1967)	0	3	0
Golub and McConnell(1968)	1	0	0	Ungar and Oceguera-Navarro (1965)	1	0	0
Golub et al.(1969)	1	0	0	Ungar (1966)	2	0	0
Golub et al.(1970)	2	0	3	Ungar and Cohen (1966)	3	1	1
Gordon et al. (1969)	0	1	0				
Greene and Kimble(1967)	0	1	0				
Gross and Carey (1965)	0	1	0				

Experimental report	+	-	0
Ungar (1967a)	3	0	0
Ungar (1967b)	2	0	0
Ungar and Irwin (1967)	6	1	0
Ungar et al. (1968)	3	0	0
Ungar (1969)	2	2	0
Ungar and Fjerdingstad (1969)	2	0	0
Ungar and Galvan (1969)	1	0	0
Weiss (1970)	1	0	0
Wolthuis (1970)	4	8	0
Wolthuis et al. (1969)	1	0	0
Zippel and Domagk (1969)	1	0	0

+.....133
-.....115
0.....15

effect could be due to the stimulus, response, stimulus sensetivity or any number of specific componants involved in learning.

In an experimental procedure it would appear that first "specificity" must be defined before an attempt is made to test for it. This may seem to be an elementary step, however, it has proven to be a difficult one.

In reviewing many studies dealing with the specificity of transfer (Rosenblatt, 1970; Ungar, 1966; Babich et al., 1965; Dyal et al., 1967) their findings appear to support the possibility that the transfer is "behaviorally specific." That is the learned behavior is transfered to the recipient, which was coded by the donor. The major barrier in answering this question is the need for the appropriate means for testing (Dyal, 1971). Again, future advances may hold the answer.

In regards to the third question of pinpointing what substance is, in fact, being transfered is also difficult to answer. The different reports from different laboratories confound this inability to arrive at a clear cut answer.

Work done by Ungar (1969) has maintained that the chemical involved "must" be a peptide. On the other hand Golub and McConnell (1968) have consistently obtained better results with RNA mixtures. Rather than review some of the earlier work which supports either the protein (Ungar, 1967) or the RNA (McConnell et al., 1968) I will suffice to say that, in general, both RNA and protein can act as transfer agents.

Golub and McConnell (1971) attempt to explain why this is an acceptable answer. A quote from their work is cited:

> Since the mechanism by which memories are coded or stored in a nerve cell must involve alteration in cellular metabolism for the cell to manufacture an altered protein it would appear that some alteration in the RNA would also have to occur. It has been suggested that memory storage may involve a change in the entire process of protein syntheses.

If this can be assumed, then either RNA or protein should be able to act as transfer agents provided that it could, upon injection, induce the same subtle change in the metabolism of the recipient as was involved in the brain of the donor animal.

As can be easily seen by the content of this last major approach the answers are by no means at hand. Regardless of the seemingly chaotic amount of research and the sometimes contrary findings, science is closer to defining learning in physiological terms than any other time in history.

Direction for Future Research

The steps which have been taken thus far in formulating a concise statement regarding the physiological correlate of learning are extensive and meaningful. In spite of this progress the ultimate question has not been fully answered. It would appear that future research is needed in specific areas, which would enable experimenters to isolate more of the involved variables. Since the memory transfer work has been considered to be the most recent advancement, this prospective research in the succeeding section, is focused on this area.

First, a reliable behavioral test is needed. The reality of the 'memory transfer' is presently based on the disagreement of the data instead of upon the reliable technique for producing the effect. A behavioral test, which is replicable between and within

the laboratories is essential (Dyal, 1971).

The second area of research is focused on whether or not the transfer effect is relevant to the learning process of the donors. To accomplish this it would be necessary to attain better controls and a more incisive demonstration of behavioral specificity. (For further explanation of this see Dyal, 1971). Also to look at other phenomenon of learning such as partial reinforcement, extinction effects etc. and determine the extent to which they are transferred would lend considerable support to the molecular theory of learning.

Another aspect previously discussed in regards to the electrical activity in the brain may also be further explored. It has been demonstrated that short term memory can be disrupted by a number of agents. Attempts have been made by Reinis (1971) to determine the effects of other agents on memory transfer. Further assessment of this and its effects will undoubtedly be beneficial to a deeper understanding of learning. It may be found that long term memory can also be disrupted by such elements, which would further clarify what may be occurring during learning.

As in a great majority of other investigations in the scientific realm, evidence will probably be found through comparative analysis From work with different species it has already been shown that some species are better to study regarding particular learning problems. This uniqueness of species raises the possibility that different mechanisms may be involved in the learning process, depending on the species. Perhaps the complex learning process of humans will not be found by comparative analysis of lower intelligence animals. Considering the prevailing experimental method involved in memory

transfer it does not seem likely that humans will be anxious to volunteer to be either "donors" or "recipients" in the too near future! However, evidence to make such a conclusion, that this uniqueness of humans is unsolvable, is by no means settled. Comparative analysis will undoubtedly continue.

These are only a few of the areas fu ure research will study. With each new experiment presently unknown areas will be uncovered. The future ultimately holds the physiological correlates of learning. Humankind must continue to think and learn about itself if an understanding of how one actually "knows" is ever to be found.

IMPLICATIONS AND APPLICATIONS

It takes little imagination to arrive at the implications and applications of knowing where and what happens during learning. Questions that have occupied the minds of psychologists, educators and those in the field of medecine may be easily answered or simplified with this knowledge.

Mental health has often been damaged by people learning adverse ways of coping, over-attending to past events which come to overshadow their entire lives or being unable to change behaviors due to little or no motivation to learn new behaviors. Could coded molecules be introduced to the brain, in such a way that new learning and selective forgetting could be accomplished? Or at another level of mental health; Could infantile autism have it's roots in "malcoded" molecule of learning or a faulty consolidation process? Could mental retardation, which plagues young and old, be prevented or cured by injection of precoded molecules?

In education, where learning is the goal, renovations may also occur. Children who suffer through school years, because they are "slow" or unable to attend to the subject matter or any other of the things that hamper learning could possibly be easily rectified with this new knowledge. A neurological examination may uncover the cause of this interference. Ultimately, depending on the disorder, perhaps science will also have the ability to remove the barrier or introduce substances which may be missing or not functioning. Again as in mental health the possibilities are vast.

Medecine has recently begun to look at the mind as being involved in medical disorders. Could it be possible to recode a person to a healthy state? Of even more importance-Could medecine and psychology unite, and if there is a learning basis for neuroses and physical maladies, assist the whole person in regaining total health?

Unfortunately, the possibility of abuse cannot be overlooked. The power of being in control of a persons learning ability is frightening. I will not venture to purpose any of these possibilities. Ones imagination can undoubtedly supply these without much difficulty.

The last few paragraphs only scratch the surface of how these years of scientific work may someday be utilized. As advances are made the reality of application will be known.

CONCLUSION

The content of the preceeding pages is confusing and controversial. Only a very few facts are relatively well established.

To confound this chaos experimental results are not always in accordance. Furthermore, the vast number of variables which are involved in the learning process serve to slow progress. Given these conditions it would seem that an atmosphere unconducive to discovery would exist. Nevertheless the commitment of researchers has apparently overcome these conditions and additions to the wealth of knowledge are being made.

I had two objectives in exploring and writing this paper. First, I personally wanted to increase my own knowledge regarding the mechanisms and functions of the brain and their relationship to the learning process. I feel learning is at the basis of all human behavior. Also, intending to someday work with children and their families any knowledge of this process could only enhance my proficiency. Secondly, I wanted to systematically report some of the past and recent findings in this area. Within this intent I hoped to possibly clarify some unanswered questions others may have. I sincerely hope I have accomplished the later of these intentions sufficiently. I am sure I have fulfilled the first.

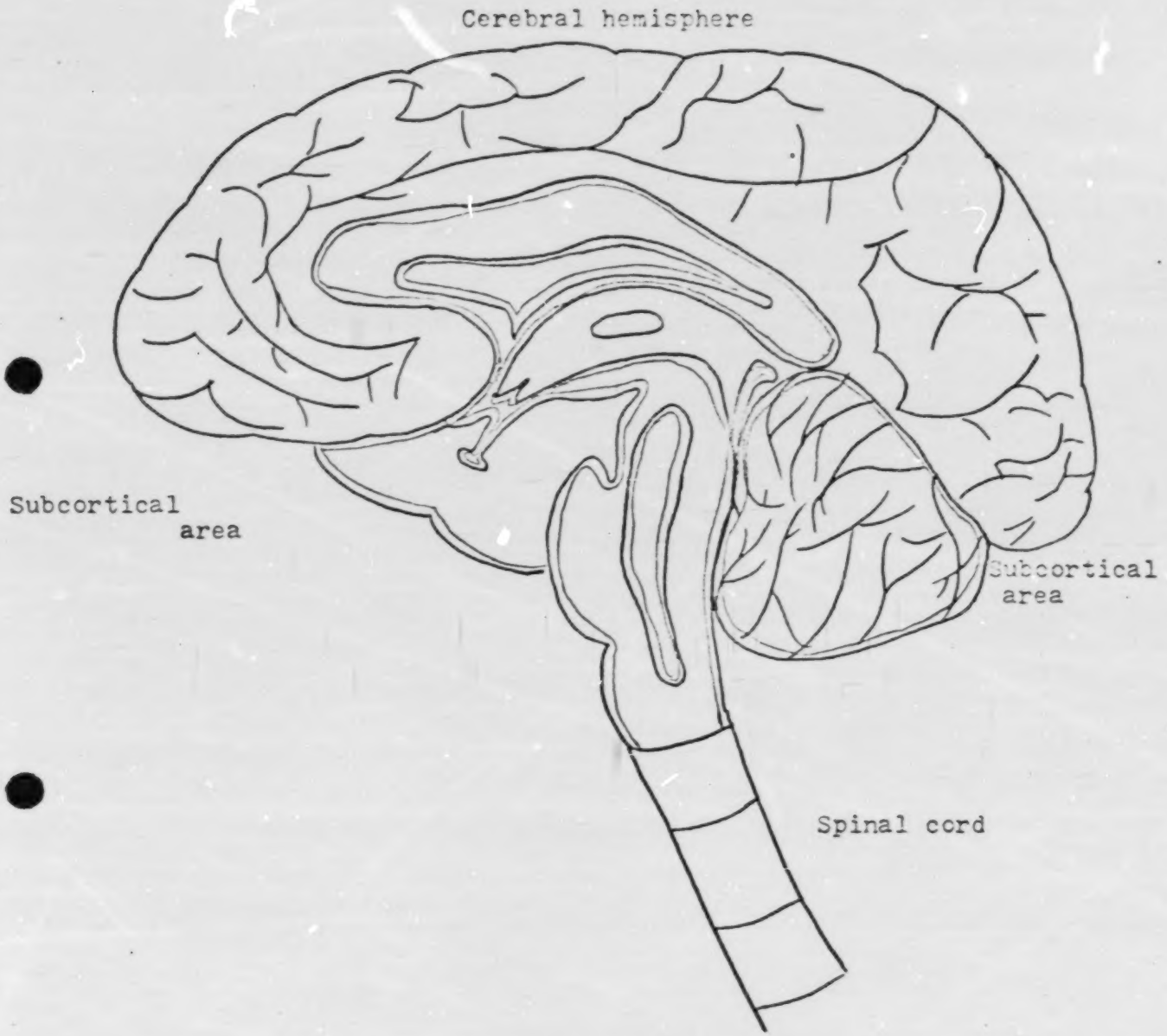


Figure 1. The three major parts of the brain

Cerebral hemisphere=black line
Subcortical area=black & grey line
Spinal cord=grey line

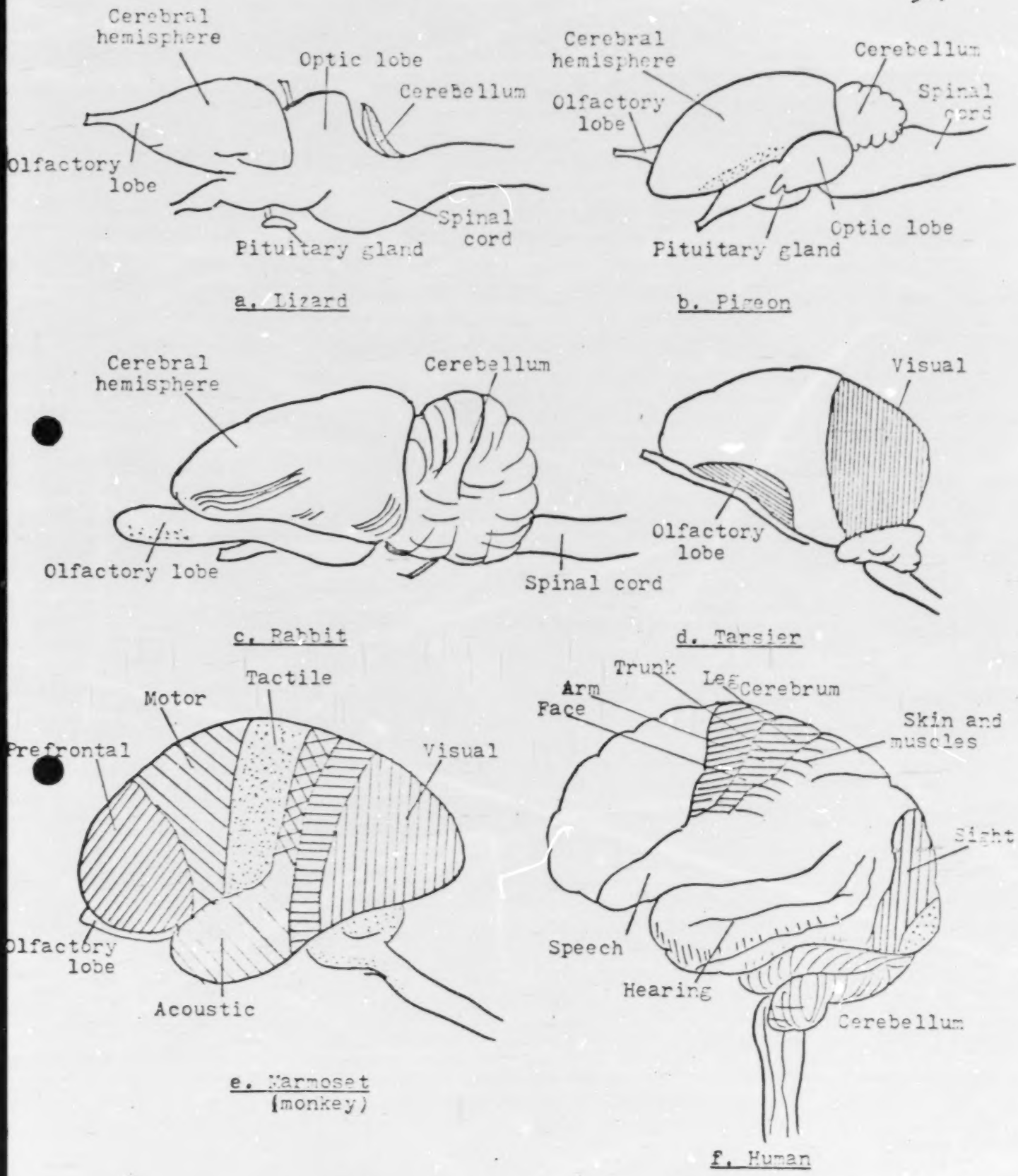


Figure 2. Progression in the anatomy of the brain from lower to higher vertebrates.

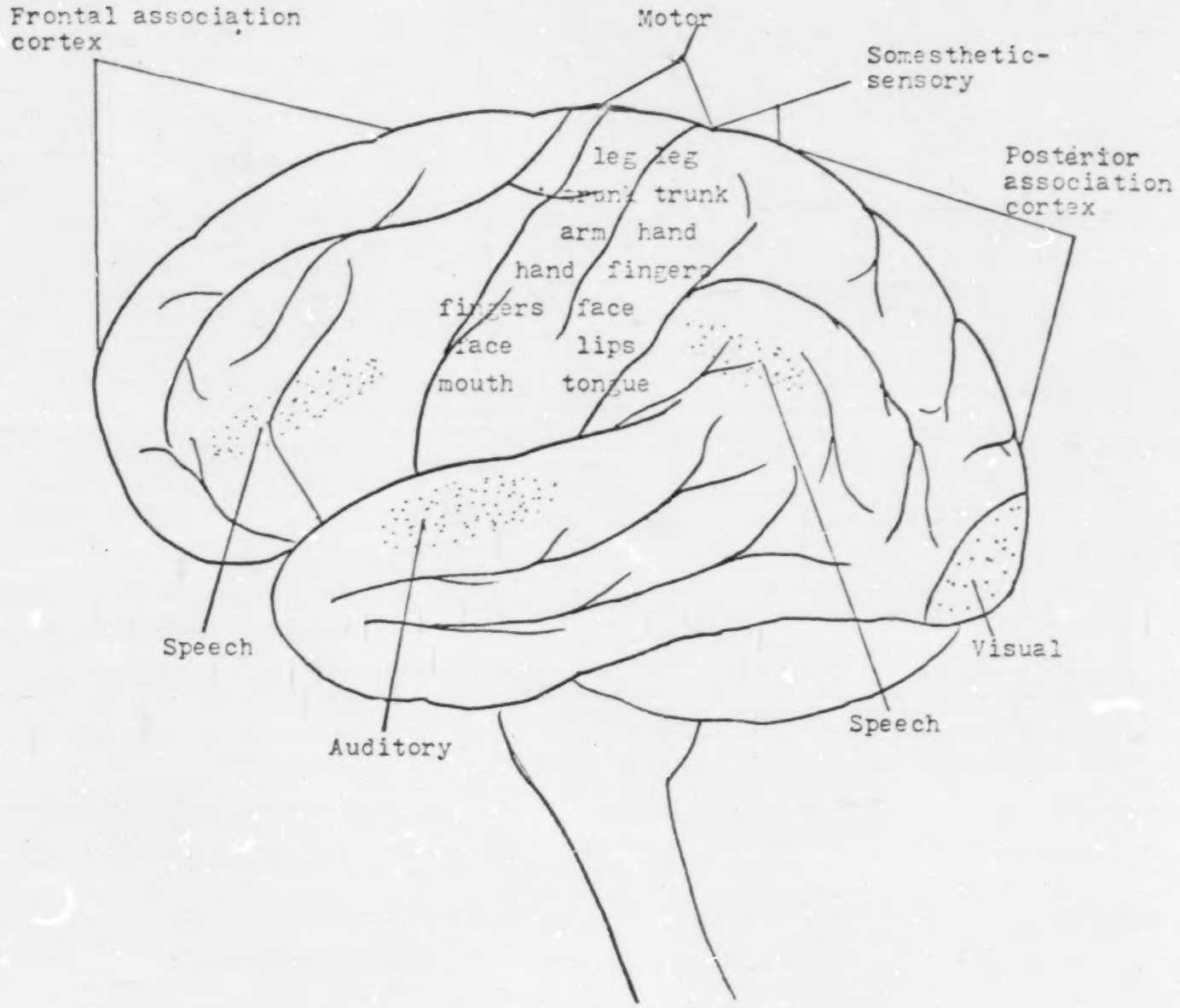


Figure 3. Association Areas
Posterior and Frontal association cortex.
(also indicated--motor and somesthetic areas
and areas important to comprehension and
production of human speech)

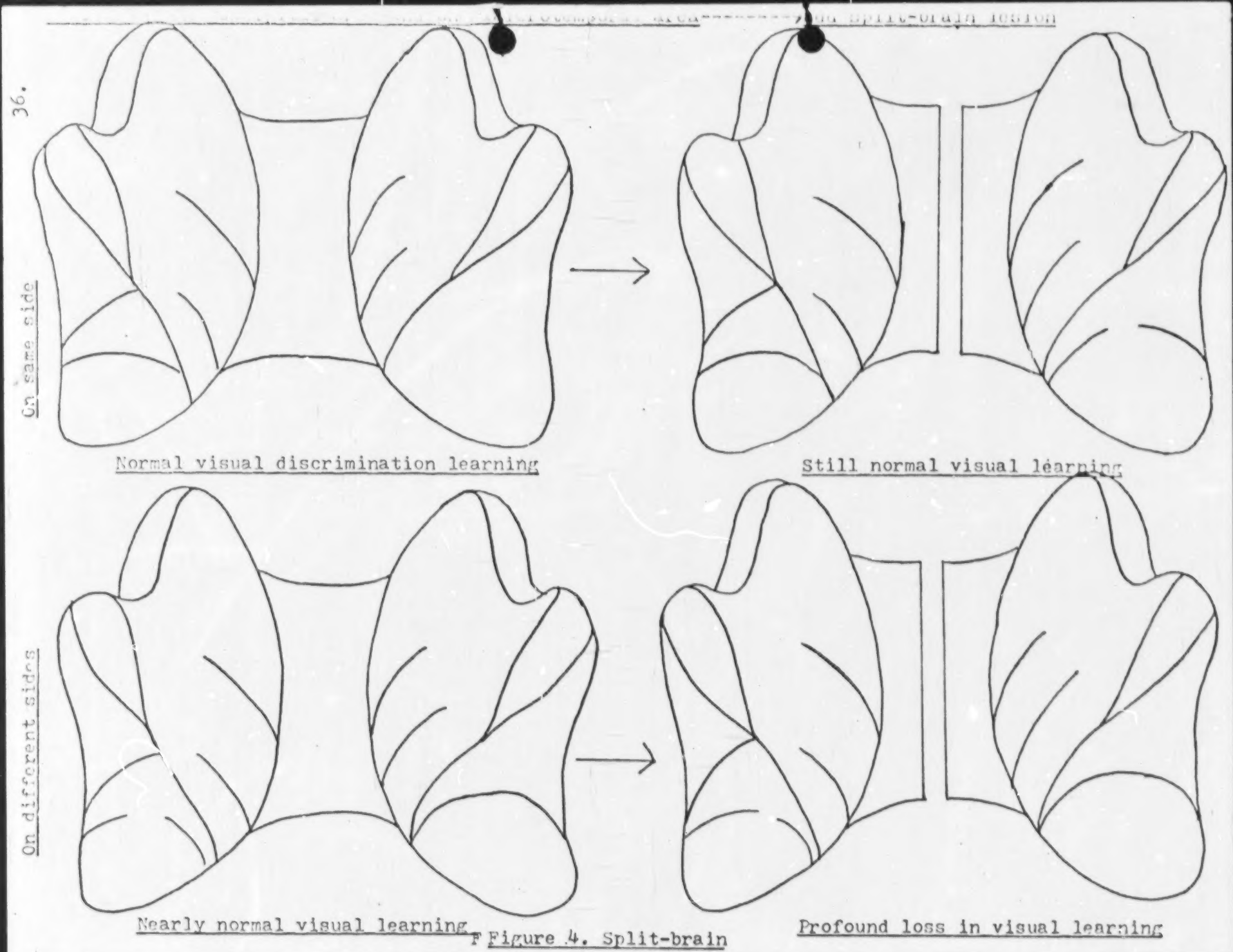


Figure 4. Split-brain

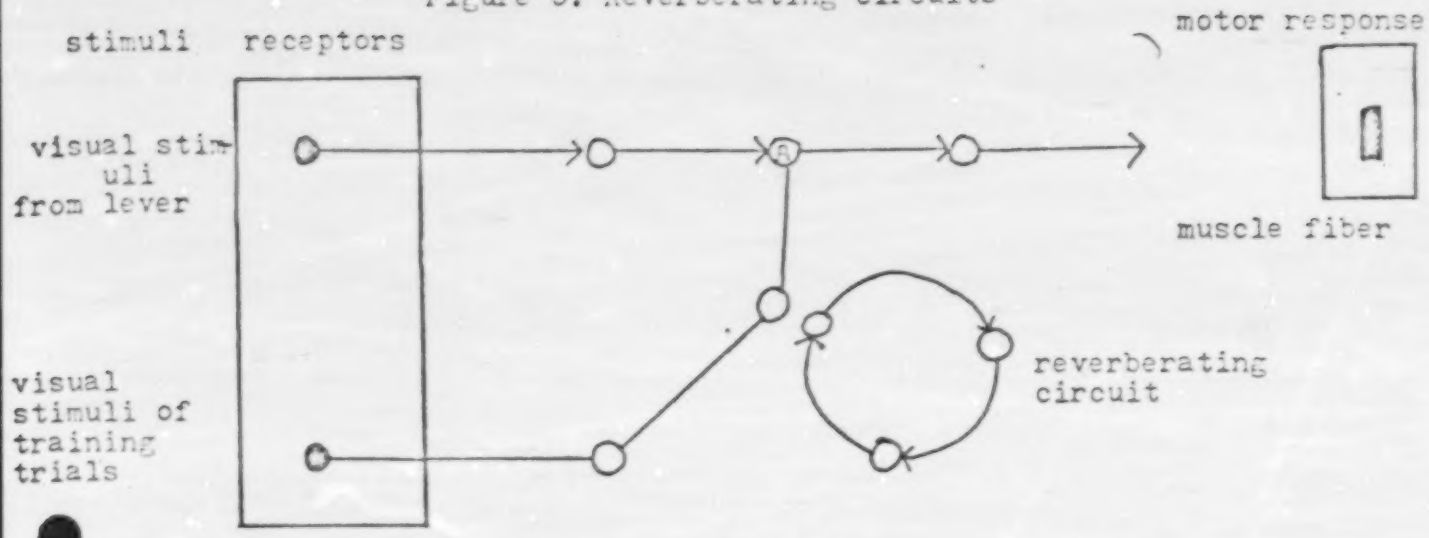
Summary of split-brain figure (4)

At least one side of the occipital cortex must be connected with the inferotemporal cortex on one side; otherwise there is a profound loss in visual discrimination learning.

Figure 4 indicates both sides of the brain; the lesions are the shaded blue areas. When the only connection is between the two different areas on different sides of the brain and thus by way of the corpus callosum (a network of nerves connecting two hemispheres), behavior may be slightly impaired (lower left). When the corpous callosum is cut learning ability is greatly impaired.(lower right). (Krech et al., 1968.)

Figure 5. The three speech areas of the cortex

Figure 6. Reverberating circuits



A neuronal model of learning (Krech et al. 1969, pp 467)

Each neuron pictured here can be stimulated into discharge by any one impulse delivered to it from a neuron that precedes it in the chain. This is not the case with neuron A , with the large cell body. This neuron has a bigger threshold; it requires two impulses presented simultaneously to provoke it into activity.

With no training there is no response. Mere sight of a lever in a learning experience could not attain the high threshold needed to activate A . However, when activity is started in the lower group of neurons, by the stimuli of the training trials, and is maintained along with impulses entering the upper chain, the response at the muscle fiber will occur. The activity coming in from the receptors along the lower neurons will not continue long after a training trial is over, unless some mechanism like a "reverberating circuit" is provided.

If neuronal activity were started in such a loop, it might continue to reverberate indefinitely, transmitting the excitatory message around and thus provide a permanent new aspect to the brain' pattern of electrical activity. This circuit would be the neural basis of the memory.

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